REMARKS

In the Office Action mailed July 18, 2008, claims 46 and 48-52 were withdrawn from consideration, and claims 1-27, 45 and 47 were rejected under 35 USC 103(a).

Amendments

Claim 1 has been amended to clarify the definition of variable R_4. This amendment is supported by the specification as filed, including the schemes and page 2, lines 15-19.

Abstract

The abstract was objected to because it was too long. In response, a substitute abstract is presented. Reconsideration and withdrawal of the objection is respectfully requested.

Declaration

Two documents were submitted in an Information Disclosure Statement on August 19, 2008. These documents are:

1) J. McConathy, L. Martarello, E. J. Malveaux, V. M. Camp, G. D. Bowers, J. J. Olson, M. M. Goodman, "FAMP and N-methyl FAMP: Fluorinated analogs of aminoisobutyric acid with high uptake in a rodent model of intracranial tumors (Abstract No. 558)," Proceedings of the SNM 48th Annual Meeting, Toronto, Ontario, Canada, June 23-27, 2001, published in J. Nuclear Medicine, May 2001 Supplement, Volume 42, Number 5, 149P

2) J. McConathy, L. Martarello, and M. M. Goodman, "Introduction of 18F at neopentyl positions via cyclic sulfamidates: Synthesis of 18F-labeled α,α-dialkyl amino acids as potential tumor imaging agents," Fourteenth international symposium on radiopharmaceutical chemistry, Interlaken Switzerland, June 10-15, 2001, published in J. Labelled Cpd. Radiopharm. 2001, Volume 44, Suppl. 1, S376-S378.

The documents disclose the synthesis of ^{18}F N-Methyl 3-fluoro-2-amino-2-methyl propanoic acid (^{18}F N-Me FAMP). Material in the documents was disclosed at two

separate conferences in June, 2001. The priority date of the current application is April 30, 2002 (provisional application 60/377,124). The priority document discloses the synthesis of ^{18}F N-Me FAMP (see page 3, lines 2-3 and Scheme 1 of provisional application 60/377,124, for example). The priority date (April 30, 2002) is less than one year before the publication of the two abstracts. Therefore, the invention was not "patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States" (35 U.S.C. 102(b)) and the publications do not qualify as 35 U.S.C. 102(b) art for the current application.

Attached to this response is a Declaration of inventor Mark Goodman stating the coauthors of the documents who are not coinventors of the current invention were acting under the direction and supervision of the coinventors. Therefore, the invention was not "known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent" (35 U.S.C. 102(a)) and the documents are not 35 U.S.C. 102(a) art against the current invention.

35 U.S.C. 103(a) rejection

Claims 1-27, 45 and 47 were rejected under 35 U.S.C. 103(a) over Goodman (US 5808146) and Christensen (J. Biol. Chem., 1965, 240(9), p. 3609-3616). Applicant traverses the rejection.

A prima facie case of obviousness is not made in this case. The Office Action states "One of ordinary skill in the art would therefore have been motivated to alkylate the amino group of the compounds of Goodman to produce N-methyl compounds for use in medical PET imaging which could be expected to show useful differences in distribution and rates of metabolic destruction. The corresponding ethylated compounds, as adjacent higher homologs of the methylated compounds, would be expected to show similar behavior and would therefore also be obvious." It is noted the Office Action only

mentions methyl and ethyl N-alkyl groups in its arguments. There is no explanation provided in the Office Action as to why changing the N-methyl or N-ethyl group to a higher alkyl group, an alkenyl group or an alkynyl group would be obvious. It is also noted that compounds containing cyclic groups are not discussed in the Office Action. Therefore, there is no reason provided for rejecting compounds having N-alkyl groups where R_4 is $-(C_kH_{2k+1})$ where k is 3-5, and where R4 is $-(C_kH_{2k-1})$ or $-(C_kH_{2k-3})$ where k = 2-5. Therefore, compounds where R_4 is $-(C_kH_{2k+1})$ where k is 3-5, and where R4 is $-(C_kH_{2k-1})$ or $-(C_kH_{2k-3})$ where k = 2-5 are believed to not be rejected. A new independent claim containing these non-rejected compounds is provided (claim 53). This claim should be allowable.

Christensen

The Office Action states "Christensen . . . teaches than [sic] N-methylation of amino acids causes them to be preferentially transported by a different route than the non-alkylated compound allowing more control of the transport of the amino acid."

The Christensen reference is misinterpreted. The Christensen reference describes the effect of adding one, two or three methyl groups to certain amino acids on the particular transport system used by the amino acid. The Christensen reference states "Introducing a single N-methyl group does not tend to decrease the reactivity of amino acids with the so-called alanine-preferring transport system of the Ehrlich cell. . . An N-methyl group largely eliminates reactivity with the so-called leucine-preferring and lysine-accepting transport systems." (Christensen, p. 3615, Summary points 1 and 2). The fact that N-methylation can be used to shift the transport system does not lead to the conclusion that "one of ordinary skill in the art would therefore have been motivated to alkylate the amino group of the compounds of Goodman to produce N-methyl compounds for use in medical PET imaging which could be expected to show useful differences in distribution and rates of metabolic destruction." The way an amino acid is transported into a tissue is not relevant to the distribution of the compound in tissues or rates of metabolic destruction, and is not indicative of the usefulness of the compound in imaging tissue.

The Office Action does not provide an explanation for why one of ordinary skill in the art would find differences in distribution of amino acids and rates of metabolic destruction to be useful in medical PET imaging.

To comply with the post-KSR interpretation of the obviousness requirement, "it remains necessary [post-KSR] to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new chemical compound." Takeda Chemical Industries, Ltd. v. Alphapharma Pty., Ltd., 492 F.3d 1350, 1357 (Fed. Cir. 2007). In this case, the Office Action states the reason is "to produce N-methyl compounds for use in medical PET imaging which could be expected to show useful differences in distribution and rates of metabolic destruction."

However, there is no reasonable expectation of success in the modification suggested. Christensen shows differential results of the transport reactivity depending on the amino acid which is N-methylated. This means that if one did combine the teachings of Christensen and US 5808146 as suggested in the Official Action, there would be no predictability in the transport affinity of such N-methylated amino acids or in the transport system used. There would also be no predictability in the use of N-methylated amino acids as tumor imaging agents based on the teachings of Christensen. There is no reason identified that would have led a chemist to modify an amino acid compound to include a methyl group for use in tumor imaging.

The claims of the current patent application are directed to non-carbon-11 radiolabeled small branched, cyclic and acyclic amino acid analogs for imaging tumors by nuclear medicine imaging as well as use in targeted radiotherapy. The Christensen reference is directed to an early (1965) investigation into attempting to determine how different amino acids enter an Ehrlich cell. The Christensen reference does not teach or mention imaging or labeling tumors, and there would be no reason to look to the teachings of the Christensen reference when trying to solve the technical problem of the current patent application. Radiohalogenation and labeling compounds with non-carbon-11

radionuclides is not straightforward. As stated in the current specification, cyclic sulfamidate precursors were required to be prepared in order to synthesize compounds of the invention (2005/0192458, paragraph 58). The cited references do not teach or suggest this synthesis system which was reported to be a key in the preparation of the claimed compounds (2005/0192458, paragraph 58). The unobviousness of a process required to produce a compound is a factor which should be considered in determining the obviousness of a compound. [In re Hoeksema (CCPA1967) 154 USPQ 169].

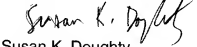
In addition, the amino-substituted compounds of the invention have surprisingly high tumor selectivity as compared to non-amino substituted compounds (see Table IV, for example).

In view of the above arguments, the claims are believed to be nonobvious over the cited references.

CONCLUSION

Reconsideration and withdrawal of the rejections and objections is respectfully requested. This response is accompanied by a Petition for Extension of Time (one month) and an authorization to charge the fee due (believed to be $130.00 for a one month extension of time for a large entity) to Deposit Account No. 07-1969. If the amount authorized to be charged is incorrect, please charge any fees required, including any extensions of time required, to Deposit Account No. 07-1969.

Respectfully submitted,



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